

CLAIMS

- 1 1. An apparatus comprising a three-dimensional (3D) array of solid-phase supports,
2 the array adapted to provide parallel synthesis of a library of molecules with 3D diversity.
- 1 2. The apparatus of claim 1, wherein the supports are functionalized.
- 1 3. The apparatus of claim 1, wherein the supports are fabricated using material
2 selected from the group consisting essentially of resin, glass, silica gel, alumina gel,
3 cellulose, plastic, polyolefins, polypropylene, polyethylene, halogenated polyolefins,
4 polytetrafluoroethylene, poly(chlorotrifluoroethylene), polyamides, polyimides,
5 poly(paraxylylenes), phenol-formaldehyde polymers, combinations thereof, and other
6 material that may be functionalized and is compatible for use in combinatorial chemistry.
- 1 4. The apparatus of claim 1, wherein individual locations in the 3D array may be
2 assigned to selected molecules in the library such that selected molecules may be
3 synthesized at and retrieved from their respective locations.
- 1 5. The apparatus of claim 1, wherein the supports comprise walls of apertures
2 formed in plates.
- 1 6. The apparatus of claim 5, wherein the 3D array comprises a plurality of plates
2 stacked with the apertures substantially aligned and the aperture walls form side walls for
3 a plurality of wells.
- 1 7. The apparatus of claim 6, wherein an end plate forms end walls of the wells.

- 1 8. The apparatus of claim 6, wherein a means for preventing cross contamination
2 between the wells is provided.
- 1 9. The apparatus of claim 1, wherein the supports are suspended within apertures
2 formed in plates.
- 1 10. The apparatus of claim 9, wherein the 3D array comprises a plurality of plates
2 stacked with the apertures substantially aligned and aperture walls form side walls for a
3 plurality of wells.
- 1 11. The apparatus of claim 10, wherein an end plate forms end walls of the wells.
- 1 12. The apparatus of claim 10, wherein a sealing mechanism to prevent cross
2 contamination between the wells is provided.
- 1 13. The apparatus of claim 10, wherein the supports are selected from the group
2 consisting essentially of mesh, rods, disks, tubes, rings, beads, sheets, and combinations
3 thereof.
- 1 14. The apparatus of claim 10, wherein a porous enclosure occupies at least a portion
2 of each aperture formed in the plates, the supports comprise beads, and the porous
3 enclosure is adapted to retaining the beads.

1 15. The apparatus of claim 14, wherein the porous enclosure occupies only a portion
2 of each aperture formed in the plates, leaving the remaining portion of each aperture as a
3 vent.

1 16. The apparatus of claim 1, wherein the 3D array comprises a plurality of discrete
2 supports arranged in a plurality of columns in one or more wells.

1 17. The apparatus of claim 16, wherein one column of supports occupies each well
2 and a plurality of wells are arranged in a two-dimensional (2D) array.

1 18. The apparatus of claim 16, wherein the supports are selected from the group
2 consisting essentially of rods, disks, tubes, rings, beads, sheets, supports adapted to being
3 stacked in a column, supports adapted to being suspended in a well by a rack, and
4 combinations thereof.

1 19. The apparatus of claim 16, wherein abutting supports in a given column are
2 adapted to being coupled together.

1 20. The apparatus of claim 16, wherein the supports comprise beads contained in
2 porous enclosures, the enclosures adapted to being stacked in a column or suspended in a
3 well by a rack.

1 21. The apparatus of claim 20, wherein the enclosures are adapted to being stacked in
2 a column and to being separated by sliding a gate between abutting enclosures.

1 22. The apparatus of claim 1, wherein the supports comprise inner walls of tubes, the
2 tubes being secured in two-dimensional (2D) frameworks, wherein the 3D array
3 comprises a plurality of such 2D frameworks of tubes stacked with the inner walls of the
4 tubes substantially aligned, and wherein the inner walls form side walls for a plurality of
5 wells.

1 23. The apparatus of claim 22, wherein a sealing mechanism to temporarily join
2 abutting tubes is provided.

1 24. The apparatus of claim 22, wherein end caps form end walls of the wells.

1 25. The apparatus of claim 1, wherein the supports are suspended within tubes, the
2 tubes being secured in two-dimensional (2D) frameworks, wherein the 3D array
3 comprises a plurality of such 2D frameworks of tubes stacked with the inner walls of the
4 tubes substantially aligned, and wherein the inner walls form side walls for a plurality of
5 wells.

1 26. The apparatus of claim 1, wherein the supports comprise beads contained in
2 porous enclosures, the porous enclosures having non-porous side walls and being secured
3 in two-dimensional (2D) frameworks, wherein the 3D array comprises a plurality of such
4 2D frameworks of porous enclosures stacked with the enclosure side walls substantially
5 aligned, and wherein the enclosure side walls form side walls for a plurality of wells.

1 27. The apparatus of claim 26, wherein the porous enclosures comprise tubes having
2 at least one mesh end wall.

1 28. The apparatus of claim 26, wherein a sealing mechanism to temporarily join
2 abutting enclosures is provided.

1 29. The apparatus of claim 26, wherein end caps form end walls of the wells.

1 30. An apparatus comprising a mechanism adapted to arranging a plurality of solid-
2 phase supports in a three-dimensional (3D) array to provide parallel synthesis of a library
3 of molecules with 3D diversity.

1 31. The apparatus of claim 30, wherein the mechanism adapted to arranging a
2 plurality of solid-phase supports in a 3D array is selected from the group consisting
3 essentially of:

4 a) a plurality of plates having apertures formed therein and stacked with the
5 apertures substantially aligned, wherein the supports comprise the aperture walls and the
6 aperture walls form side walls for a plurality of wells;

7 b) a plurality of plates having apertures formed therein and stacked with the
8 apertures substantially aligned, wherein the supports are suspended within the apertures
9 and aperture walls form side walls for a plurality of wells;

10 c) a plurality of discrete supports arranged in a plurality of columns in one or
11 more wells;

12 d) a plurality of tubes having inner walls and being secured in two-dimensional
13 (2D) frameworks, wherein a plurality of such 2D frameworks of tubes may be stacked
14 with the inner walls of the tubes substantially aligned, wherein the inner walls may form
15 side walls for a plurality of wells, and wherein the supports comprise the inner walls of
16 the tubes; and

17 e) a plurality of porous enclosures having non-porous side walls and being
18 secured in two-dimensional (2D) frameworks, wherein a plurality of such 2D frameworks
19 of porous enclosures may be stacked with the enclosure side walls substantially aligned,
20 wherein the enclosure side walls may form side walls for a plurality of wells, and wherein
21 the supports comprise beads contained in the porous enclosures.

1 32. The apparatus of claim 30, wherein the supports are functionalized.

1 33. An apparatus comprising a support transfer device adapted to enable transfer of
2 solid-phase supports used in a three-dimensional (3D) array of solid-phase supports, the
3 array adapted to provide parallel synthesis of a library of molecules with 3D diversity.

1 34. The apparatus of claim 33, wherein the 3D array comprises a plurality of discrete
2 supports arranged in a plurality of columns in one or more wells.

1 35. The apparatus of claim 34, wherein the supports are adapted to being suspended in
2 a well by a rack and the support transfer device is a rack comprising:

- 3 a) a plurality of rods sized to be inserted through an aperture formed in each
4 support; and
5 b) a mechanism to prevent the supports from coming off the rack.

1 36. The apparatus of claim 35, wherein the rack additionally comprises a mechanism
2 to keep the supports immersed in liquid.

1 37. The apparatus of claim 35, wherein the mechanism to prevent the supports from
2 coming off the rack comprises an end cap attached to one end of at least one rod.

1 38. The apparatus of claim 36, wherein the mechanism to keep the supports immersed
2 in liquid comprises an obstruction device that limits movement of the supports on the
3 rods.

1 39. The apparatus of claim 33, wherein the 3D array comprises a plurality of discrete
2 supports arranged in a plurality of columns and one column of supports occupies each of
3 a plurality of wells arranged in a two-dimensional (2D) array.

1 40. The apparatus of claim 39, wherein the support transfer device comprises a
2 plurality of tubes connected at a first end of the tubes to a manifold, the tubes being
3 adapted each to suction at a second end of the tube one support taken from each column
4 of supports in the 3D array when a vacuum is applied to the manifold.

1 41. The apparatus of claim 39, wherein the support transfer device comprises:
2 a) a transfer block having a plurality of recesses, the recesses being sized to
3 receive one or more support and being spaced to substantially align with at least a portion
4 of the plurality of wells of the 3D array; and
5 b) at least one gate slidably engaged with the transfer block, each gate having
6 apertures formed therein, wherein sliding the gate into an open position allows one or
7 more supports to pass through apertures in the gate and sliding the gate into a closed
8 position withholds supports from passing through the gate.

1 42. The apparatus of claim 40, wherein the plurality of tubes are spaced to
2 substantially align with the plurality of wells of the 3D array and second end of each tube
3 comprises a cavity shaped to capture the support at the second end of the tube.

1 43. The apparatus of claim 41, wherein the at least one gate comprises one gate and
2 vacuum orifices extend from the recesses to allow withdrawing of air from the recesses,
3 thereby suctioning supports into the recesses when the gate is in an open position.

1 44. The apparatus of claim 41, wherein the at least one gate comprises two gates and
2 the supports may enter through one gate and exit through the other gate.

1 45. The apparatus of claim 41, wherein the at least one gate comprises three gates,
2 supports may enter a first portion of each recess through an upper gate, supports may exit
3 the first recess portion and enter a second portion of each recess through a first lower
4 gate, supports may exit the second recess portion through a second lower gate, the first
5 recess portion is sized to receive a column of a plurality of supports, and the second
6 recess portion is sized to receive one support from each column of supports within the
7 first recess portion.

- 1 46. A method comprising the steps of:
2 a) functionalizing a plurality of solid-phase supports;
3 b) placing the plurality of supports in a three-dimensional (3D) array; and
4 c) performing parallel synthesis of a library of molecules in the 3D array of
5 supports with 3D diversity.
- 1 47. The method of claim 46, wherein a step of attaching a R_1 group member to each
2 support is performed before the step of placing the plurality of supports in the 3D array.
- 1 48. The method of claim 46, wherein the step of placing the plurality of supports
2 comprises using a support transfer device.
- 1 49. The method of claim 46, additionally comprising the step of removing the
2 plurality of supports from the 3D array with a support transfer device.
- 1 50. The method of claim 46, additionally comprising the step of cleaving molecules
2 from selected supports.
- 1 51. The method of claim 47, wherein the supports in the 3D array are arranged in a
2 plurality of planes stacked in a Z direction and wherein the step of placing the plurality of
3 supports in the 3D array comprises assigning at least one unique R_1 group member to
4 each plane.

1 52. The method of claim 48, wherein the support transfer device is selected from the
2 group consisting essentially of:
3 a) a rack having a plurality of rods sized to be inserted through an aperture formed
4 in each support and a mechanism to prevent the supports from coming off the rack;
5 b) a plurality of tubes connected at a first end of the tubes to a manifold, the tubes
6 being adapted each to suction at a second end of the tube one support taken from each
7 column of supports in the 3D array when a vacuum is applied to the manifold; and
8 c) a transfer device including:
9 i) a transfer block having a plurality of recesses, the recesses being sized to
10 receive one or more support and being spaced to substantially align with a
11 plurality of wells of the 3D array; and
12 ii) at least one gate slidably engaged with the transfer block, each gate
13 having apertures formed therein, wherein sliding the gate into an open position
14 allows one or more supports to pass through apertures in the gate and sliding the
15 gate into a closed position withholds supports from passing through the gate.

1 53. The method of claim 49, wherein the support transfer device is selected from the
2 group consisting essentially of:

3 a) a rack having a plurality of rods sized to be inserted through an aperture formed
4 in each support and a mechanism to prevent the supports from coming off the rack;

5 b) a plurality of tubes connected at a first end of the tubes to a manifold, the tubes
6 being adapted each to suction at a second end of the tube one support taken from each
7 column of supports in the 3D array when a vacuum is applied to the manifold; and

8 c) a transfer device including:

9 i) a transfer block having a plurality of recesses, the recesses being sized to
10 receive one or more support and being spaced to substantially align with a
11 plurality of wells of the 3D array; and

12 ii) at least one gate slidably engaged with the transfer block, each gate
13 having apertures formed therein, wherein sliding the gate into an open position
14 allows one or more supports to pass through apertures in the gate and sliding the
15 gate into a closed position withholds supports from passing through the gate.

1 54. The method of claim 49, wherein the step of removing the plurality of supports
2 comprises removing one Z plane at a time.

1 55. The method of claim 51, wherein the least one unique R1 group member
2 comprises one unique R1 group member.
